

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning on page 4, line 6 with the following paragraph:

The present invention describes a method for improving [[of]] the bioavailability and half-life of 7-keto-DHEA. Frequent dosing of the hormone is needed when given as an oral supplement because much of the hormone is negated during its first pass through the liver. Therefore, improved supplements containing various effective substituted .DELTA.5-androstenes are needed.

Please replace the paragraph beginning on page 5, line 3 with the following paragraph:

The hormone DHEA is a naturally produced steroid in humans which is produced in the adrenals glands, testes, and brain. DHEA is the most abundant circulating hormone in humans but circulating levels decline significantly in late adulthood. ~~Circulating levels of will~~ and continue to decrease with age ~~for unknown reasons~~. This phenomena has ~~lead~~ led many to suggest that maintaining levels of DHEA may counteract many of the pathophysiological effects of aging. Because the FDA considers it a naturally occurring vitamin, the sale of DHEA is unregulated. It has been available over-the-counter as a nutritional supplement since the mid 1990s.

Please replace the paragraph beginning on page 6, line 1 with the following paragraph:

However, individuals with normal levels of DHEA who take high doses of DHEA are likely to experience unwanted side effects because the hormone is readily converted into androgens such as estrogen and testosterone. Patients (with normal adrenal function) who have taken supplemental DHEA have demonstrated the following side effects: hair loss, increased facial hair growth, acne (in over 50% of patients), increased perspiration and odor, scalp itching, menstrual irregularities, irritability and restlessness. Moreover, the long term effects of high

levels of DHEA are largely unknown. ~~And studies~~ Studies have produced data suggesting that high levels of DHEA may increase the risk of breast and prostate cancer. Other studies have correlated high levels of DHEA with increased blood pressure and other cardiovascular risk factors. DHEA has been modified to produce various .DELTA.5-androstenes for producing the desired effects while minimizing side effects. The present invention relates to a modified form of the hormone[,,] 7-keto-dehydroepiandrosterone.

Please replace the paragraph beginning on page 6, line 20 with the following paragraph:

Unlike DHEA and other steroids, 7-keto-DHEA is not metabolized into estrogens or testosterone. Because ~~7-keto-DHEA~~ of this, supplemental 7-Keto-DHEA DHEA treatment often yields the desirable effects of DHEA treatment without the unwanted side effects. ~~Thus 7-keto-DHEA has no androgenic or estrogenic side effects—the hormonal side effects are absent.~~

Please replace the paragraph beginning on page 9, line 18 with the following paragraph:

The currently known benefits of 7-keto-DHEA occur at doses in the range of 350 to 1400 mg/day. The supplement is rather expensive at the present time, and its benefits are similar to those of DHEA. 7-keto-DHEA differs from DHEA in its side effects: it does not get converted to estrogens and testosterone in the body, so estrogenic and androgenic side effects are considered to be fewer than for DHEA. These side effects (breast enlargement, acne, growth of body and facial hair) occur only in ~~aminority~~ a minority of users; for those in whom they do, the additional cost may be justified, while for others it would not.

Please replace the paragraph beginning on page 10, line 5 with the following paragraph:

DHEA and other .DELTA.5-androstenes (including 7-keto-DHEA) are extensively metabolized to hydroxylated intermediates in the liver by cytochrome ~~P45family~~ P45 family of

drug metabolizing enzymes. Ingesting DHEA as an oral supplement requires frequent dosing because much of the hormone is negated during its first pass through the liver. ~~The bioavailability~~ Bioavailability and half-life have not been established for 7-keto-DHEA. As with most other steroidal hormones, micronization improves bioavailability. The presence of other substances that use the same metabolic enzymes can improve bioavailability or half-life, but can also cause side effects.

Please replace the paragraph beginning on page 10, line 13 with the following paragraph:

~~We have~~ I have discovered that 7-keto-DHEA may be modified to improve oral bioavailability and plasma half-life in humans and mammals. Specifically, 7-keto-DHEA is modified at the 3.^{sup.rd} carbon, the 17.^{sup.th} carbon, or at both 3.^{sup.rd} carbon and the 17.^{sup.th} carbons with one or more of the following: tetrahydropyranyl (both mono and di-ethers), 1-methoxycyclopentane (both mono and di-ethers), cyclopent-1'-enyl (both mono and di-ethers), or combinations thereof. These modifications make the DHEA molecule more lipophilic, permitting circulation through the lymphatic system rather than its normal route. This permits the hormone to induce its desired effect while avoiding rapid metabolism by the liver.

Please replace the paragraph beginning on page 10, line 22 with the following paragraph:

~~But as~~ As late as the 1960's and 70's ~~the push was still on~~ work was ongoing to develop effective oral steroids that were not 17-alpha alkylated and did not carry the same unwanted risks of liver toxicity. One concept that was successfully pursued was the notion of bypassing the liver altogether. To do this ~~we need~~ it is desirable to change the way the steroid is absorbed by the body, so that it will enter circulation through the lymphatic system and not by its normal route. The lymphatic system is responsible for the absorption and distribution of dietary fats, and shuttles these nutrients from the intestines to the lymph nodes so that they can reach peripheral tissues without having to first pass through the liver. To effectively do this however ~~we need to~~ increase the fat solubility of the compound needs to be increased considerably, either by adding a

carboxylic acid ester (normally used to create injectable compounds) or an ether group. For ~~our~~ purposes of the invention ~~we can look at~~ esters and ethers as serve essentially the same ~~thing~~ role. The key point with both structural additions is that they increase the lipid solubility of the steroid, and therefore the likelihood that it will be absorbed by the lymphatic system with dietary fat, yet later break off in circulation (via esterase enzymes) to yield an intact active hormone.

Please replace the paragraph beginning on page 12, line 16 with the following paragraph:

Among the compounds ~~in~~ of the invention are:

Please replace the paragraph beginning on page 16, line 13 with the following paragraph:

~~With the~~ The compounds of the present invention will provide a substantial increase in oral bioavailability and plasma half life in mammals as compared to non-modified .DELTA.5-androstene compounds. Furthermore, advantageous treatment with one or more compounds of the present invention will improve a subject's memory, improve neurological health, improve weight loss by increasing fat reduction, increase energy, reduce fatigue, improve immune response, increase T3 thyroid hormone activity, and combinations thereof.

Please replace the paragraph beginning on page 16, line 19 with the following paragraph:

Although the invention has been described with reference to one or more preferred embodiments, this description is not to be construed in a limiting sense. There ~~is modification~~ are modifications of the disclosed embodiments, as well as alternative embodiments of this invention, which will be apparent to persons of ordinary skill in the art, and the invention shall be viewed as limited only by reference to the following claims.